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Green, efficient and practical Michael addition of arylamines to α,β-unsaturated ketones

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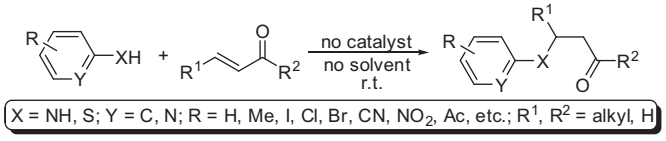
ABSTRACT

The aza-Michael addition of aromatic amines to α,β-unsaturated ketones was carried out effectively at room temperature in good to excellent yields without any catalyst or solvent. It was significant that part of adducts could be collected in almost quantitative yield without column chromatography. This procedure offered a green, efficient, and practical approach for the synthesis of β-amino ketones.

1. Introduction

The β-amino carbonyl moiety is always found in biological products and pharmaceutically active substances.[1] Over the past decades, many approaches have been developed for the synthesis of this skeleton. Among these methods, the aza-Michael addition is preferable due to its atom economy, high selectivity, and simple processes. A great deal of catalyst systems have been explored to date for the transformation[2] using Lewis acids (In,[3] Yb,[4] Cu,[5] Bi,[6] Fe,[7] Sm,[8] molecular Iodine,[9] Pd,[10] etc.), Brønsted acids,[11] base,[12] ionic liquid,[13] and others.[14] However, most of these catalyst systems suffer from limitations including harsh reaction conditions with low yields, tedious workup procedures and the necessity of column chromatography for purification. On the other hand, the elimination or reduction of hazardous solvents in chemical processes is becoming more and more desirable in pursuit of 'Green Chemistry'.[15] Quite recently, practical procedures in absence of solvents[16] or catalysts[17,22] have been accomplished. However, the development of greener system for the aza-Michael addition in both catalyst- and solvent-free conditions, to the best of our knowledge, is still an ongoing challenge. Our previous work showed that secondary aliphatic amines could react with chalcones to achieve adducts in excellent yields with the promotion of ultrasound irradiations.[18a] Although it was remarkable that no catalyst or solvent was required in these reactions, the aromatic amines were demonstrated to be almost inert in the reaction possibly as a result of their weaker nucleophilicity.[4,12,13,14b] On the other hand, the selectivity of mono-addition and di-addition was challenge in catalytic systems. In our continuing efforts to develop green procedures for the 1,4-conjugated addition,[18] we herein disclose an efficient approach for the mono-addition of aromatic amines to α,β-unsaturated ketones with high selectivity, which performs at room temperature in absence of any catalyst or solvent (Scheme 1). In addition, the most often-used purification methods of column chromatography and recrystallization are not necessary for many of our cases at all. Significantly, the neat product can be obtained over 2 g in one relatively large-scaled experiment. It is expected to be potentially applied in industrial processes.



Scheme 1.

2. Results and discussion

Initially, a template reaction using the 1:1.3 M ratio of 4-chloroaniline and but-3-en-2-one was selected to optimize the solvent condition at room temperature (Fig. 1, see the detailed data in

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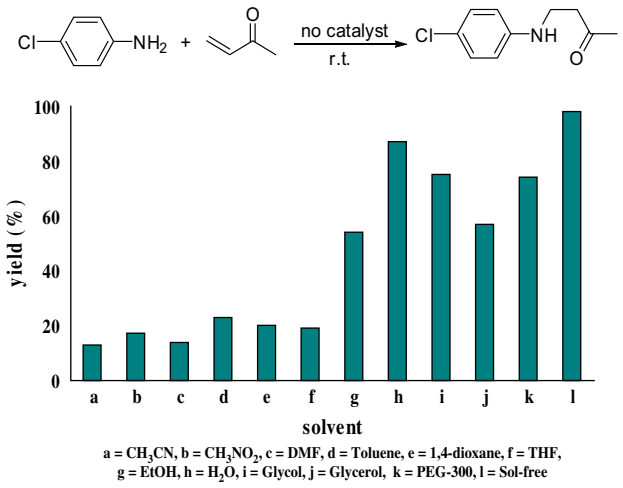
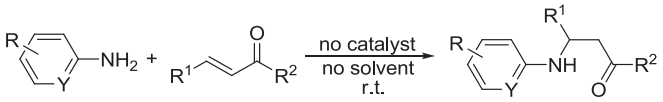


Fig. 1.

Supplementary data). It was found that the reaction could proceed successfully in the absence of a catalyst when MeCN was used as the solvent, although the desired product was isolated in a very low yield. Encouraged by this result, we subsequently screened other common solvents including CH_3NO_2, DMF, toluene, 1,4-dioxane, THF and EtOH (Fig. 1, a–g). It was surprising that only protic solvent EtOH could offer a moderate yield. Consequently, other protic solvents, such as H_2O, glycol, glycerol, and PEG-300 were introduced to increase the yield of the final product. As expected, an obvious improvement in yields was observed from 54% to 87% when the reaction was carried out in these solvents, respectively (Fig. 1, h–k). Considering the fact that the template reaction runs better in protic solvents than in aprotic solvents, the hydrogen bond between substrate and solvent is supposed to play an important role. Therefore, the neat reaction of 4-chloroaniline with but-3-en-2-one was examined, which was expected to work even better than was dispersed by solvents. The reaction proceeded smoothly and specifically, just as we supposed, to afford the desired product in almost quantitative yield. When our case is compared with other workup procedures, such as column chromatography or recrystallization, only a simple operation for the removal of the excessive but-3-en-2-one in vacuo would lead to neat product (Fig. 1, l).

With the optimal condition, we subsequently investigated the scope of the aromatic amines (**2a**–**n**). As seen from Table 1, the reactions offered moderate to excellent yields for the β-amino carbonyl compounds when the substituted anilines were introduced. Among the anilines selected, those bearing the chloro- (**2b**), bromo-(**2c**), iodo-(**2d**), and methyl (**2f**) substituent at the

Table 1
Aza-Michael addition of aromatic amines to α,β-unsaturated ketones[a]



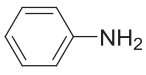
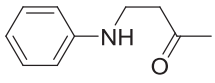
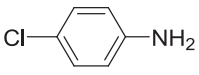
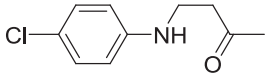
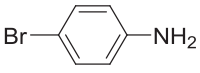
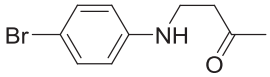
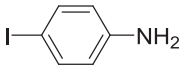
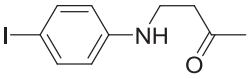
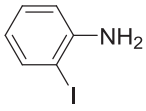
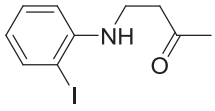
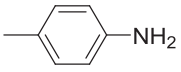
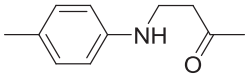
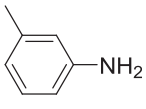
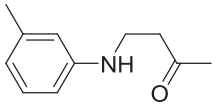
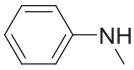
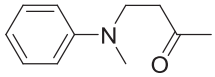
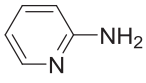
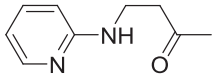
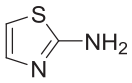
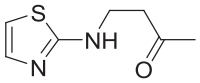
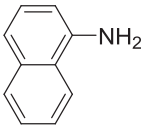
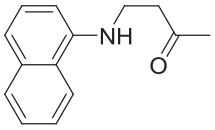
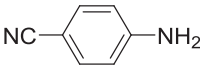
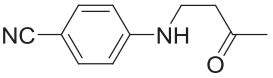
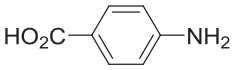
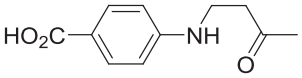
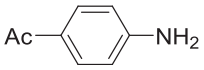
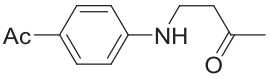
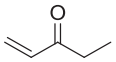
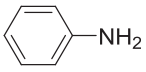
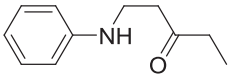
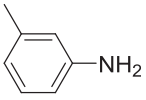
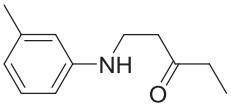
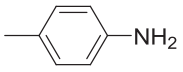
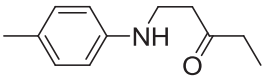
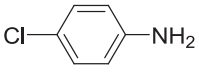
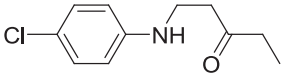
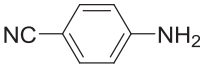
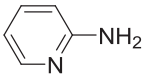
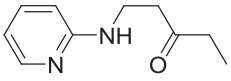
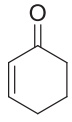
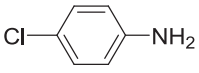
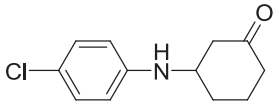
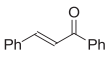
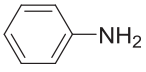
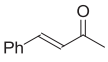
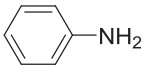
Entry	α,β-unsaturated ketones	Ar–NH_2	Product	Time(h)	Yield(%)[b]
1	 **1a**	 **2a**	 **3aa**	6	84
2		 **2b**	 **3ab**	3	98[c]
3		 **2c**	 **3ac**	4	96[c]
4		 **2d**	 **3ad**	4	98[c]
5		 **2e**	 **3ae**	4	51
6		 **2f**	 **3af**	4	97[c]
7		 **2g**	 **3ag**	6	98[c]
8		 **2h**	 **3ah**	24	64
9		 **2i**	 **3ai**	4	97[c]

Table 1 (*continued*)

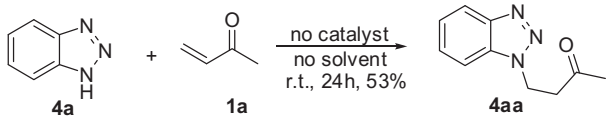
Entry	α,β-unsaturated ketones		Ar–NH_2		Product		Time(h)	Yield(%)[b]
10				**2j**		**3aj**	4	91
11				**2k**		**3ak**	6	98[c]
12				**2l**		**3al**	10	64
13				**2m**		**3am**	24	79
14				**2n**		**3an**	24	73
15		**1b**		**2a**		**3ba**	5	81
16				**2g**		**3bg**	10	97[c]
17				**2f**		**3bf**	2	99[c]
18				**2b**		**3bb**	10	96[c]
19				**2l**	––	––	24	––
20				**2i**		**3bi**	8	98[c]
21		**1c**		**2b**		**3cb**	48	94
22		**1d**		**2a**	––	––	24	––
23		**1e**		**2a**	––	––	24	––

[a] Reaction conditions: amines (1.0 mmol), α,β-unsaturated ketones (1.3 mmol), room temperature.
[b] Yield of isolated product after flash chromatography.
[c] Yield of pure product without column chromatography.

para-position reacted with but-3-en-2-one (**1a**) to give the corresponding pure products in almost quantitative yield without any need of column chromatography or recrystallization (Table 1, entries 2–4, 6). Similar result was obtained as well in the reaction of *meta*-toluidine with **1a** (Table 1, entry 7). The steric effect for anilines with *ortho*-iodo (**2e**) and *N*-methyl (**2h**) substituents (Table 1, entries 5, 8) was observed obviously, which was illustrated by their lower reactivity than aniline (**2a**) (Table 1, entry 1). It should be noted that the hetero-aromatic amines, pyridin-2-amine (**2i**) (Table 1, entry 9) and thiazol-2-amine (**2j**) (Table 1, entry 10), could also react well to give the desired products **3ai** and **3aj** in 97% and 91% yields, respectively. Meanwhile, 4-(naphthalen-1-ylamino)butan-2-one (**3ak**) could be obtained in a 98% yield through the reaction of naphthalen-1-amine (**2k**) and **1a**. However, when the anilines

containing electron-withdrawing groups (Table 1, entries 12–14) were utilized as nucleophiles, the corresponding adducts were provided in lower yields even after prolonged reaction time. It may be attributed to the poorer nucleophilicity of these amines.

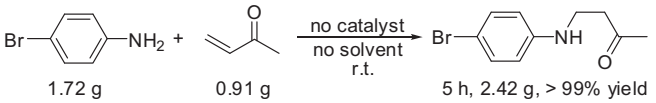
In order to examine the generality of enones, pent-1-en-3-one (**1b**) and cyclohex-2-enone (**1c**) were introduced as well. Fortunately, the methyl-(**2g**, **2f**) and chloro-(**2b**) substituted anilines as well as hetero-aromatic amine (**2i**) reacted with **1b** to give the adducts quantitatively without an extra purification process. As to the cyclic vinylketone **1c**, less reactivity than **1b** was observed, which offered the desired product in 94% yield. Similarly, as a result of the negative influence from the strong electron-withdrawing group on the nucleophilicity of amino group, the reaction of 4-aminobenzonitrile (**2l**) and **1b** didn't occur under the same conditions (Table 1, entry 19). Study on wider generality for enones and amines were carried out. It was found that introduction of phenyl group into enone molecules hampered the reaction greatly, which was well demonstrated in the reactions of chalcone (**1d**) or 4-phenylbut-3-en-2-one (**1e**) with **2a**. As to phenylvinylketone, an analog of **1d**, only poor reactivity was observed in the standard reaction, no expected product was isolated after workup. Combination of benzylamine and but-3-en-2-one (**1a**) also led to the similar result. Notably, the reaction between 1*H*-benzo[*d*][1,2,3] triazole (**4a**) and **1a** could also carry out smoothly to give the N-alkylation product (**4aa**) in 53% yield under standard condition (Scheme 2).



4a 1a 4aa

Scheme 2.

Since this mild and green protocol is of a relatively wide generality for the syntheses of β-arylamino ketones, it would be potentially useful in industrial processes if the reactions could be scaled up. Therefore, a large-scaled reaction of 4-bromoaniline (**2c**) (10.0 mmol) with **1a** (13.0 mmol) was carried out (Scheme 3). To our delight, the reaction was completed in 5 h to give the neat product of **3ac** in 99% yield only after the removal of excessive **1a** under the reduced pressure.



1.72 g 0.91 g 5 h, 2.42 g, > 99% yield

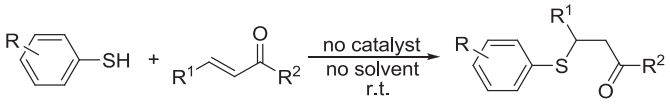
Scheme 3.

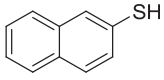
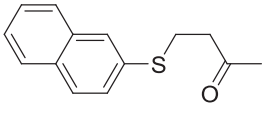
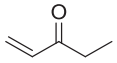
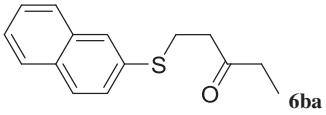
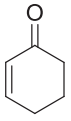
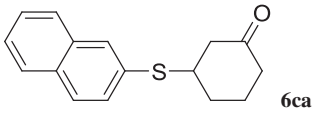
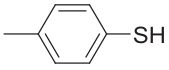
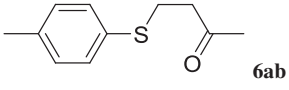
In an endeavor to expand the scope of the methodology, some other nucleophiles were tested to give the data as listed in Table 2. It is satisfying that naphthalene-2-thiol (**5a**) could react smoothly with **1a**, **1b**, and **1c** to produce the β-sulfido carbonyl compounds in moderate to good yields (Table 2, entries 1–3). However, an analog of **5a**, 4-methylbenzenethiol (**4b**) showed less reactivity to give the corresponding adduct (**6ab**) in an 88% yield after 24 h (Table 2, entry 4).

3. Conclusion

In summary, we have disclosed an environmentally benign procedure for the synthesis of the β-arylamino ketones using the aza-Michael addition of aromatic amines to α,β-unsaturated ketones. Some obvious advantages of this transformation are demonstrated: (1) the reactions could proceed successfully without any catalyst and solvent, thus avoiding the use of expensive or sensitive

Table 2
Thia-Michael addition of thiophenol to α,β-unsaturated ketones[a]



Entry	Substrate		Product	Time(h)	Yield(%)[b]
1	 **5a**	 **1a**	 **6aa**	2	90
2		 **1b**	 **6ba**	1	99[c]
3		 **1c**	 **6ca**	10	73
4	 **5b**	 **1a**	 **6ab**	24	88

[a] Reaction conditions: thiols (1.0 mmol), α,β-unsaturated ketones (1.3 mmol), room temperature.
[b] Yield of isolated product after flash chromatography.
[c] Yield of pure product without column chromatography.

catalysts and toxic organic solvents; (2) the workup is greatly simplified for the neat products in almost quantitative yields without need of column chromatography in most of cases; (3) there was no decrease in yield when the reaction was extended to gram scales.

4. Experimental section

4.1. General

^{1}H NMR spectra were recorded on a Varian INOVA 400 and and ^{13}C NMR were recorded on a Varian INOVA 75 or 100 MHz spectrometer using $CDCl_3$ as solvent and TMS as internal standard. High resolution mass spectra were obtained using Micromа GCT-TOF instrument.

4.2. Typical experimental procedure for the reaction of aromatic amines to α,β-unsaturated ketones

Aromatic amines (1.0 mmol) and α,β-unsaturated ketones (1.3 mmol) were added into a round-bottom flask. Then the mixture was stirred at room temperature in air, until amines were completely consumed (checked by TLC) or an appropriate time. Upon the completion of reaction, the excessive α,β-unsaturated ketones were evaporated under the reduced pressure to give the neat adducts. For the uncompleted reaction, the residue was purified by flash column chromatography.

4.3. Typical experimental procedure for the reaction of aromatic thiols to α,β-unsaturated ketones

Aromatic thiols (1.0 mmol) and α,β-unsaturated ketones (1.3 mmol) were added into a round-bottom flask. Then the mixture was stirred at room temperature in air, until thiols were completely consumed (checked by TLC) or an appropriate time. Upon the completion of reaction, the excessive α,β-unsaturated ketones were evaporated under the reduced pressure to give the neat adducts. For the uncompleted reaction, the residue was purified by flash column chromatography.

*4.3.1. 4-(Phenylamino)butan-2-one (**3aa**)*[11c]. ^{1}H NMR (400 MHz, $CDCl_3$): δ=2.15 (s, 3H), 2.74 (t, J=6.1 Hz, 2H), 3.41 (t, J=6.1 Hz, 2H), 3.96 (s, 1H, NH), 6.60 (d, J=7.9 Hz, 2H), 6.71 (t, J=7.3 Hz, 1H), 7.17 (t, J=7.9 Hz, 2H) ppm. HRMS (m/z): $[M]^+$, calcd for $C_{10}H_{13}NO$: 163.0997, found: 163.0997.

*4.3.2. 4-(4-Chlorophenylamino)butan-2-one (**3ab**)*[19]. ^{1}H NMR (400 MHz, $CDCl_3$): δ=2.17 (s, 3H, CH_3), 2.74 (t, J=6.0 Hz, 2H), 3.38 (t, J=6.0 Hz, 2H), 4.13 (s, 1H, NH), 6.53 (d, J=8.8 Hz, 2H), 7.12 (d, J=8.8 Hz, 2H) ppm. HRMS (m/z): $[M]^+$, calcd for $C_{10}H_{12}{}^{35}ClNO$: 197.0607, found: 197.0607.

*4.3.3. 4-(4-Bromophenylamino)butan-2-one (**3ac**).* ^{1}H NMR (400 MHz, $CDCl_3$): δ=2.17 (s, 3H), 2.74 (t, J=6.0 Hz, 2H), 3.38 (t, J=6.0 Hz, 2H), 4.04 (s, 1H, NH), 6.48(d, J=8.6 Hz, 2H), 7.24 (d, J=8.7 Hz, 2H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$) δ=208.1, 146.8, 132.1, 114.7, 109.2, 42.4, 38.5, 30.5 ppm. HRMS (m/z): [M]+, calcd for $C_{10}H_{12}{}^{79}BrNO$: 241.0102, found: 241.0102.

*4.3.4. 4-(4-Iodophenylamino)butan-2-one (**3ad**).* ^{1}H NMR (400 MHz, $CDCl_3$): δ=2.16 (s, 3H), 2.73 (t, J=6.0 Hz, 2H), 3.38 (t, J=5.9 Hz, 2H), 4.06 (s, 1H, NH), 6.39 (d, J=8.8 Hz, 2H), 7.41(d, J=8.8 Hz, 2H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$) δ=208.1, 147.3, 137.8, 115.2, 78.1, 42.3, 38.2, 30.5 ppm. HRMS (m/z): $[M]^+$, calcd for $C_{10}H_{12}INO$: 288.9964, found: 288.9964.

*4.3.5. 4-(2-Iodophenylamino)butan-2-one (**3ae**)*[20]. ^{1}H NMR (400 MHz, $CDCl_3$): δ=2.19 (s, 3H), 2.79 (t, J=6.4 Hz, 2H), 3.47 (t, J=6.4 Hz, 2H), 4.42 (s, 1H, NH), 6.45 (t, J=7.5 Hz, 1H), 6.58 (d, J=8.1 Hz, 1H), 7.21 (t, J=7.1 Hz, 1H), 7.66 (d, J=7.8 Hz, 1H) ppm. HRMS (m/z): $[M]^+$, calcd for $C_{10}H_{12}INO$: 288.9964, found: 288.9969.

*4.3.6. 4-(p-Tolylamino)butan-2-one (**3af**)*[21]. ^{1}H NMR (400 MHz, $CDCl_3$): δ=2.15 (s, 3H), 2.23 (s, 3H), 2.74 (t, J=6.0 Hz, 2H), 3.39 (t, J=4.2 Hz, 2H), 653 (d, J=9.2 Hz, 2H), 6.99 (d, J=7.3 Hz, 2H) ppm. HRMS (m/z): $[M]^+$, calcd for $C_{11}H_{15}NO$: 177.1154, found: 177.1154.

*4.3.7. 4-(m-Tolylamino)butan-2-one (**3ag**)*[17f]. ^{1}H NMR (400 MHz, $CDCl_3$): δ=2.16 (s, 3H), 2.27 (s, 3H), 2.74 (t, J=5.9 Hz, 2H), 3.40 (t, J=6.1 Hz, 2H), 6.42 (d, J=7.6 Hz, 2H), 6.54 (d, J=7.5 Hz, 1H), 7.06 (t, J=8.0 Hz, 1H) ppm. HRMS (m/z): $[M]^+$, calcd for $C_{11}H_{15}NO$: 177.1154, found: 177.1155.

*4.3.8. 4-(Methyl(phenyl)amino)butan-2-one (**3ah**)*[19]. ^{1}H NMR (400 MHz, $CDCl_3$): δ=2.15 (s, 3H), 2.70 (t, J=7.0 Hz, 2H), 2.92 (s, 3H), 3.63 (t, J=7.0 Hz, 2H), 6.70–6.74 (m, 3H), 7.22–7.26 (m, 2H) ppm. HRMS (m/z): $[M]^+$, calcd for $C_{11}H_{15}NO$: 177.1154, found: 177.1155.

*4.3.9. 4-(Pyridin-2-ylamino)butan-2-one (**3ai**).* ^{1}H NMR (400 MHz, $CDCl_3$): δ=2.16 (s, 3H, CH_3), 2.77 (t, J=6.0 Hz, 2H), 3.60 (t, J=6.0 Hz, 2H), 4.82 (s, 1H, NH), 6.36 (d, J=8.4Hz, 1H), 6.54 (t, J=5.8 Hz, 1H), 7.37 (t, J=6.8 Hz, 1H), 8.06 (d, J=8.0 Hz, 1H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ=208.6, 158.4, 147.9, 137.5, 112.9, 108.0, 43.2, 36.4, 30.5 ppm. HRMS (m/z): $[M]^+$, calcd for $C_9H_{12}N_2O$: 164.0950, found: 164.0951.

*4.3.10. 4-(Thiazol-2-ylamino)butan-2-one (**3aj**).* ^{1}H NMR (400 MHz, $CDCl_3$): δ=2.18 (s, 3H), 2.83 (t, J=5.8 Hz, 2H), 3.60 (t, J=5.7 Hz, 2H), 5.57 (s, 1H, NH), 6.48 (d, J=3.7 Hz, 1H), 7.10 (d, J=3.0 Hz, 1H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ=208.0, 170.1, 139.0, 106.5, 42.6, 40.2, 30.4 ppm. HRMS (m/z): $[M]^+$, calcd for $C_7H_{10}N_2OS$: 170.0514, found: 170.0514.

*4.3.11. 4-(Naphthalen-1-ylamino)butan-2-one (**3ak**)*[21]. ^{1}H NMR (400 MHz, $CDCl_3$): δ=2.20 (s, 3H), 2.89 (t, J=6.1 Hz, 2H), 3.60 (t, J=6.1 Hz, 2H), 6.63 (d, J=7.5 Hz, 1H), 7.25 (d, J=7.7 Hz, 1H), 7.35 (t, J=7.9 Hz, 1H), 7.42–7.45 (m, 2H), 7.77–7.79 (m, 2H) ppm. HRMS (m/z): $[M]^+$, calcd for $C_{14}H_{15}NO$: 213.1154, found: 213.1156.

*4.3.12. 4-((3-Oxobutyl) amino)benzonitrile (**3al**).* ^{1}H NMR (400 MHz, $CDCl_3$): δ=2.19 (s, 3H), 2.76 (t, J=5.9 Hz, 2H), 3.45 (t, J=5.9 Hz, 2H), 6.55 (d, J=8.7 Hz, 2H), 7.42 (d, J=8.7 Hz, 2H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ=207.8, 151.0, 134.0, 120.6, 112.4, 98.9, 42.3, 37.6, 30.5 ppm. HRMS (m/z): $[M]^+$, calcd for $C_{11}H_{12}N_2O$: 188.0950, found: 188.0949.

*4.3.13. 4-((3-Oxobutyl)amino)benzoic acid (**3am**)*[22]. ^{1}H NMR (400 MHz, DMSO-d_6): δ=2.11 (s, 3H), 2.71 (t, J=6.6 Hz, 2H), 3.25 (t, J=6.6 Hz, 2H), 6.38 (br s, 1H), 6.54 (d, J=8.7 Hz, 2H), 7.66 (d, J=8.7 Hz, 2H) ppm. HRMS (m/z): $[M]^+$, calcd for $C_{11}H_{13}NO_3$: 207.0895, found: 207.0896.

*4.3.14. 4-((4-Acetylphenyl)amino)butan-2-one (**3an**).* ^{1}H NMR (400 MHz, $CDCl_3$): δ=2.50 (s, 3H), 2.18 (s, 3H), 2.77 (t, J=5.9, 2H), 3.49 (t, J=5.9 Hz, 2H), 4.59 (s, 1H, NH), 6.55 (d, J=8.7 Hz, 2H), 7.82 (d, J=8.7 Hz, 2H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ=207.8, 196.5, 151.8, 131.0, 126.8, 111.5, 42.4, 37.7, 30.4, 26.1 ppm. HRMS (m/z): $[M]^+$, calcd for $C_{12}H_{15}NO_2$: 205.1103, found: 205.1103.

*4.3.15. 1-(Phenylamino)pentan-3-one (**3ba**)*[23]. ^{1}H NMR (400 MHz, $CDCl_3$): δ=1.05 (t, J=7.3 Hz, 3H), 2.44 (q, J=7.3 Hz, 2H), 2.72 (t, J=6.1 Hz, 2H), 3.42 (t, J=6.1 Hz, 2H), 6.61 (d, J=7.2 Hz, 2H), 6.71

(t, J=5.8 Hz, 1H), 7.17 (t, J=7.9 Hz, 2H) ppm. HRMS (m/z): $[M]^+$, calcd for $C_{11}H_{15}NO$: 177.1154, found: 177.1154.

*4.3.16. 1-(m-Tolylamino)pentan-3-one (**3bg**).* ^{1}H NMR (400 MHz, $CDCl_3$): δ=1.05 (t, J=7.3 Hz, 3H). 2.27 (s, 3H), 2.44 (q, J=7.3 Hz, 2H), 2.71 (t, J=6.1 Hz, 2H), 3.41 (t, J=6.2 Hz, 2H), 6.41–6.43 (m, 2H), 6.54 (d, J=7.4 Hz, 1H), 7.06 (t, J=7.5 Hz, 1H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ=210.9, 147.8, 139.0, 129.2, 118.5, 113.9, 110.2, 41.3, 38.5, 36.3, 21.6, 7.6 ppm. HRMS (m/z): $[M]^+$, calcd for $C_{12}H_{17}NO$: 191.1310, found: 191.1309.

*4.3.17. 1-(p-Tolylamino)pentan-3-one (**3bf**).* ^{1}H NMR (400 MHz, $CDCl_3$): δ=1.05 (t, J=7.3 Hz, 3H), 2.23 (s, 3H), 2.43 (q, J=7.3 Hz, 2H), 2.71 (t, J=6.1 Hz, 2H), 3.40 (t, J=6.1 Hz, 2H), 6.54 (d, J=8.4 Hz, 2H), 6.99 (d, J=8.1 Hz, 2H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ=211.2, 145.5, 129.9, 127.0, 113.4, 41.1, 39.0, 36.4, 20.5, 7.9 ppm. HRMS (m/z): $[M]^+$, calcd for $C_{12}H_{17}NO$: 191.1310, found: 191.1306.

*4.3.18. 1-(4-Chlorophenylamino)pentan-3-one(**3bb**).* ^{1}H NMR (400 MHz, $CDCl_3$): δ=1.06 (t, J=7.3 Hz, 3H), 2.42–2.47 (m, 2H), 2.72 (t, J=6.1 Hz, 2H), 3.39 (t, J=6.1 Hz, 2H), 6.56 (d, J=8.8 Hz, 2H), 7.12 (d, J=8.8 Hz, 2H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ=210.9, 146.4, 129.2, 122.2, 114.2, 41.1, 38.7, 36.5, 7.9 ppm. HRMS (m/z): $[M]^+$, calcd for $C_{11}H_{14}ClNO$: 211.0764, found: 211.0762.

*4.3.19. 1-(Pyridin-2-ylamino)pentan-3-one(**3bi**).* ^{1}H NMR (400 MHz, $CDCl_3$): δ=1.06 (t, J=7.3 Hz, 3H), 2.44 (q, J=7.3 Hz, 2H), 2.75 (t, J=6.0 Hz, 2H), 3.62 (q, J=6.1 Hz, 2H), 4.83 (s, 1H, NH), 6.37 (d, J=8.4 Hz, 1H), 6.54–6.57 (m, 1H), 7.36–7.40 (m, 1H), 8.07 (d, J=5.0 Hz, 1H) ppm. ^{1}H NMR (75 MHz, $CDCl_3$): δ=211.2, 158.4, 148.0, 137.3, 112.8, 107.8, 41.8, 36.5, 36.4, 7.8 ppm. HRMS (m/z): $[M]^+$, calcd for $C_{10}H_{14}N_2O$: 178.1106, found: 178.1110.

*4.3.20. 3-(4-Chlorophenylamino)cyclohexanone (**3cb**)[19].* ^{1}H NMR (400 MHz, $CDCl_3$): δ=1.64–1.80 (m, 2H), 2.00–2.09 (m, 1H), 2.14–2.17 (m, 1H), 2.25–2.45 (m, 3H), 2.78–2.83 (m, 1H), 3.37 (s, 1H, NH), 3.70–3.77 (m, 1H), 6.51 (d, J=8.8 Hz, 2H), 7.10 (d, J=8.8 Hz, 2H). HRMS (m/z): $[M]^+$, calcd for $C_{12}H_{14}ClNO$: 223.0764, found: 223.0768.

*4.3.21. 4-(1H-Benzo[d][1,2,3]triazol-1-yl)butan-2-one (**4aa**).* ^{1}H NMR (400 MHz, $CDCl_3$): δ=2.18 (s, 3H), 3.27 (t, J=6.5 Hz, 2H), 4.84 (d, J=6.5 Hz, 2H), 7.35 (t, J=7.6 Hz, 1H), 7.49 (t, J=7.6 Hz, 1H), 7.63 (d, J=8.4 Hz, 1H), 8.01 (d, J=8.4 Hz, 1H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ=169.9, 127.8, 124.4, 120.2, 110.1, 43.0, 42.6, 30.6 ppm. HRMS (m/z): $[M]^+$, calcd for $C_{10}H_{11}N_3O$: 189.0902, found: 189.0901.

*4.3.22. 4-(Naphthalen-2-ylthio)butan-2-one (**6aa**)[24].* ^{1}H NMR (400 MHz, $CDCl_3$): δ=2.15 (s, 3H, CH_3), 2.81 (t, J=7.3 Hz, 2H), 3.24 (t, J=7.4 Hz, 2H), 7.41–7.50 (m, 3H), 7.74–7.81 (m, 4H) ppm. HRMS (m/z): $[M]^+$, calcd for $C_{14}H_{14}OS$: 230.0765, found: 230.0763.

*4.3.23. 1-(Naphthalen-2-ylthio)pentan-3-one (**6ab**).* ^{1}H NMR (400 MHz, $CDCl_3$): δ=1.05 (t, J=7.3 Hz, 3H), 2.41 (q, J=7.3 Hz, 2H), 2.78 (t, J=7.3 Hz, 2H), 3.25 (t, J=7.3 Hz, 2H), 7.40–7.50 (m, 3H), 7.74–7.80 (m, 4H) ppm. HRMS (m/z): $[M]^+$, calcd for $C_{15}H_{16}OS$: 244.0922, found: 244.0921.

*4.3.24. 3-(Naphthalen-2-ylthio)cyclohexanone (**6ca**)[13c].* ^{1}H NMR (400 MHz, $CDCl_3$): δ=1.70–1.83 (m, 2H), 2.14–2.21 (m, 2H), 2.31–2.46 (m, 3H), 2.71–2.75 (m, 1H), 3.52–3.57 (m, 1H), 7.48–7.50 (m, 3H), 7.78–7.83 (m, 3H), 7.91 (s, 1H) ppm. HRMS (m/z): $[M]^+$, calcd for $C_{16}H_{16}OS$: 256.0922, found: 256.0924.

*4.3.25. 4-(p-Tolylthio)butan-2-one (**6ab**)[24].* ^{1}H NMR (400 MHz, $CDCl_3$): δ=2.13 (s, 3H), 2.32 (s, 3H), 2.73 (t, J=7.3 Hz, 2H), 3.08 (t, J=7.3 Hz, 2H), 7.11 (d, J=8.2 Hz, 2H), 7.26 (d, J=2 Hz, 2H) ppm. HRMS (m/z): $[M]^+$, calcd for $C_{11}H_{14}OS$: 194.0765, found: 194.0764.

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Supplementary data

Supplementary data related to this article can be found online at doi:10.1016/j.tet.2011.03.082.

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